

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark  
Office  
(Box PCT)  
Crystal Plaza 2  
Washington, DC 20231  
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 08 January 1999 (08.01.99)	
<b>International application No.</b> PCT/GB98/01395	<b>Applicant's or agent's file reference</b> M96/0693/PCT
<b>International filing date</b> (day/month/year) 22 May 1998 (22.05.98)	<b>Priority date</b> (day/month/year) 22 May 1997 (22.05.97)
<b>Applicant</b> FREESTONE, Primrose, Pamela, Elaine et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
09 December 1998 (09.12.98)

☐ in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer P. Regis</p> <p>Telephone No.: (41-22) 338.83.38</p>
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REC'D 04 AUG 1999

WIPO PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference M96/0693/PCT	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB98/01395	International filing date (day/month/year) 22/05/1998	Priority date (day/month/year) 22/05/1997
International Patent Classification (IPC) or national classification and IPC C12N1/38		
Applicant UNIVERSITY OF LEICESTER et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 5 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand  09/12/1998	Date of completion of this report  29.07.99
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. (+49-89) 2399-0 Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer  Moonen, P  Telephone No. (+49-89) 2399 8538 



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB98/01395

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-28 as originally filed

**Claims, No.:**

1-16 as originally filed

**Drawings, sheets:**

1/12-12/12 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB98/01395

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes:	Claims	1-16
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-16
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-16
	No:	Claims	

**2. Citations and explanations**

**see separate sheet**



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/GB98/01395

Reference is made to the following documents:

**D1:** FEMS Microbiol Lett **139** (1996) 155-9; cited in the application

**D2:** J Bacteriol **177** (1995) 6989-92

**D3:** Nature **362** (1993) 446-448; cited in the application

**Introduction:**

1. Bacterial autoinducers of growth are known from the prior art:

**D1** has disclosed an autoinducer from E coli having a MW of 10,000 as indicated by preliminary experiments utilizing preparative ultrafiltration.

**D2** concerns different autoinducers from P aeruginosa of the homoserine lactone type.

**D3** refers in Figure 2 to low molecular weight homoserine lactone derivatives containing a lipophilic acyl chain as autoinducer (also mentioned in the description; see e.g. page 1 last full paragraph).

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

2. The present invention concerns the isolation of a low molecular weight autoinducer (AI) obtainable from E.coli, having a number of established properties (e.g. see Table 5 of the specification), although the chemical formula has not yet been established. The AI of the present application is differentiated from the known AI, referred to in D2-D3 as well as other obvious compounds like a known siderophore.

With respect to D1, it is noted that in the present application in step 1 (see page 13, first paragraph) the AI is bound to a factor with MW of around 10 kDa and may be separated therefrom by several procedures (e.g. heat-treatment). D1 is therefore considered to be the closest state of the art, as in D1 the complex has



**INTERNATIONAL PRELIMINARY  
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only be isolated.

3. An inventive step for the presently purified and characterized AI of E coli is recognised (Article 33(3) PCT). As the structure of the AI is not known, it is considered that **all** the properties of the AI as referred to in dependent claims 2 and 3 and including the MW <500 Da mentioned in Table 5 are essential to the invention and should be present in all the independent claim on file (including the independent claims 5 and 15); see Article 6 PCT and Rule 6.3(b) PCT. No other AI than the AI with the above mentioned essential technical features has been disclosed, i.e. it is not clearly supported by the application if the autoinducer of present claim 1 refers to a family of different autoinducers.

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## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>M96/0693/PCT</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/GB 98/ 01395</b>	International filing date (day/month/year) <b>22/05/1998</b>	(Earliest) Priority Date (day/month/year) <b>22/05/1997</b>
Applicant <b>UNIVERSITY OF LEICESTER et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☐ Certain claims were found unsearchable (see Box I).

2. ☐ Unity of invention is lacking (see Box II).

3. ☐ The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing

☐ filed with the international application.

☐ furnished by the applicant separately from the international application,

☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

☐ Transcribed by this Authority

4. With regard to the title, ☐ the text is approved as submitted by the applicant

☒ the text has been established by this Authority to read as follows:

**E. COLI, SALMONELLA OR HAFNIA AUTOINDUCERS**

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is:

Figure No. \_\_\_\_\_ ☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.



## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 98/01395

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N1/38 C12P1/04 C12P13/04 //(C12P1/04,C12R1:01,  
C12R1:19,C12R1:42)

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C12P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LYTE M ET AL: "Production of an autoinducer of growth by norepinephrine cultured Escherichia coli 0157:H7." FEMS MICROBIOL LETT, JUN 1 1996, 139 (2-3) P155-9, XP002078986 NETHERLANDS cited in the application	
A	MCKENNEY D ET AL: "Influence of Pseudomonas aeruginosa exoproducts on virulence factor production in Burkholderia cepacia: evidence of interspecies communication." J BACTERIOL, DEC 1995, 177 (23) P6989-92, XP002078987 UNITED STATES --- -/--	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

29 September 1998

Date of mailing of the international search report

12/10/1998

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Espen, J



## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 98/01395

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>ZHANG L ET AL: "Agrobacterium conjugation and gene regulation by N-acyl-L-homoserine lactones"</p> <p>NATURE, vol. 362, 1993, pages 446-448, XP002078988 LONDON GB</p> <p>-----</p>	